GENERAL DISCUSSION: SESSION IV*

HERBERT POLLACK, M.D., Ph.D., *moderator*

Professor Emeritus of Clinical Medicine
George Washington University
Washington, D.C.

JOSEPH B. DAVIS, M.D., RICHARD JOHNSON, M.D.,
JAMES W. FRAZER, Ph.D., AND RICHARD REIS, M.S.

DR. HERBERT POLLACK: Before opening the general discussion, Dr. Gandhi will discuss some recent developments in electromagnetic applicators for local and whole body hyperthermia.

DR. OM P. GANDHI (University of Utah): I shall discuss two aspects: first, the development of lower frequency broad band applicators to obtain deeper heating of tissues and, second, preliminary development of an electromagnetic applicator for whole body hyperthermia. In spite of widespread use of 2,450 and 915 MHz electromagnetic energy to produce local hyperthermia, depths of penetration are extremely limited at these frequencies. At high microwave frequencies a substantial fraction of the total energy is absorbed at the skin. At lower frequencies, particularly frequencies of the order of 300-500 MHz., there is significant reduction in energy deposition in the skin and most of the energy is thus imparted to inlying tissue. This is also apparent when one considers depths of penetration at various frequencies reported in Johnson and Guy's article. Local hyperthermia applicators at lower frequencies are therefore needed. Some applicators developed by Bio-Systems Design of Salt Lake City are described in Table I. The VSWR less than two means 90% transfer efficiency over a wide range of 200 to 550 MHz. Dimensions of the various applicators can be as low as required. In fact, they have fabricated a wide variety of applicators with dimensions as low as two inches by one and a half inches to six and one half by four inches. An interesting and very wide band applicator is that given in D (Table I). The measured VSWR for this parallel-type applicator is shown in the figure. Part of the problem in the past was that at lower frequencies the typical wave guide type

*Presented as part of a *Symposium on Health Aspects of Nonionizing Radiation* sponsored by the Subcommittee on Public Health Aspects of Energy of the Committee on Public Health of the New York Academy of Medicine and held at the Academy April 9 and 10, 1979.

TABLE I. SOME TYPICAL APPLICATORS FOR LOCAL HYPERTHERMIA

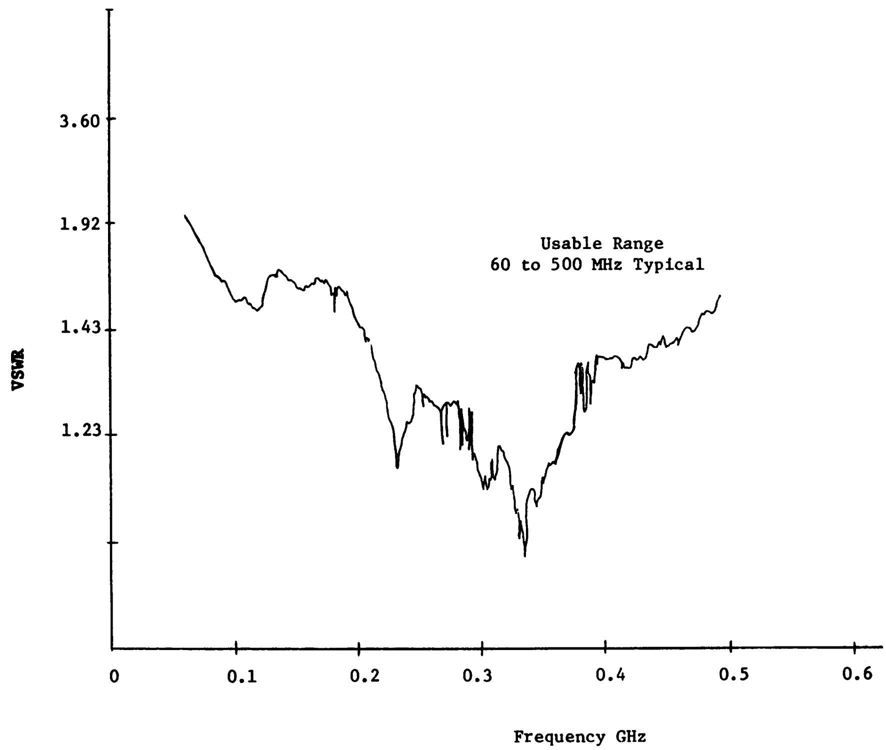
	Aperture dimensions
Dielectric loaded waveguides	
A. 200-550 MHz. VSWR ≤ 2 (10 dB return loss)	4″ × 5″
B. 650-1500 MHz. VSWR ≤ 2	2″ × 1.5″
Shaped field applicator for uniform heating	
C. 400-600 MHz. VSWR ≤ 2	6.5″ × 4″
Broadband parallel-plate applicator	
D. 60-500 MHz. VSWR ≤ 2	4″ × 5″

Each of the above applicators can, of course, be scaled up or down for a different frequency band of operation.

applicators were too big to be of much use, a problem alleviated in parallel-plate type applicators which can be made with aperture dimensions as small as desired.

Salient features of the BSD-1000 system that the Bio-Systems Design markets are shown in Table II. Important characteristics of the system are: 50 to 1,000 MHz. (expandable to higher frequencies), frequency stability, microprocessor control of up to 100 watt output, power stability, and the transfer efficiency of better than 90%. They have designed several applicators and are willing to design others to physician specifications for special applications. The biological feedback is provided by up to six nonperturbing temperature probes, each with a diameter of about 1 mm. to 1.5 mm. We hope that the semiconductor band gap type temperature probe under development at the University of Utah will be available before long and will be useful for such applications. This probe has a tip diameter less than 1 mm.

Low frequencies on the order of 75-150 MHz. offer the advantage of heating from the inside out rather than by blood-mediated outside-in heating methods presently employed. Another advantage of an electromagnetic whole body hyperthermia system is that one may be able to heat the patient to temperatures of the order of 106-108°F. in about half an hour, rather than two hours as at present. We do, however, need applicators capable of relatively uniform electromagnetic energy deposition (within about 2:1). Although my physician friends say that perhaps there is



Wide band applicator-human abdominal match 14 by 14 cm. heating area typical

not that much need for uniform heating, I think that there is some merit in not loading the hemodynamic system more than it ought to be and relatively uniform rates of energy deposition should help in that regard. An applicator we have looked at, with a reduced scale biological-phantom-filled model, is a parallel-plate end-terminated applicator that yields fairly uniform rates of energy deposition. Work presently continues to improve the uniformity and energy transfer efficiency of such applicators.

MR. EDWARD HUNT (Walter Reed Army Institute of Research): I have been impressed by the relation between research in designing applications and feedback to the science and biology of microwaves from use of these applications. This is an extremely important transfer of information between applications research and basic science.

My second comment relates to microwave tomography, having to do with the properties of the interrogating energy. With microwaves the

TABLE II. SALIENT FEATURES OF THE BIO-SYSTEMS DESIGN, INC., HYPERTHERMIA SYSTEM

Microwave	
Frequency range	50-1,000 MHz.
Expandable to	10-2,500 MHz.
Frequency stability	0.1 MHz. (Microprocessor controlled)
RF power	85-100 W
Power stability	0.5 W (Microprocessor controlled)
Power transfer efficiency:	Up to 95%
Number of available applicators	7 (to cover the 50-1,000 MHz. band, and also allow a variety of aperture dimensions from 4 x 5 cm. to 10 x 15 cm.)
Reflected power	Less than 10% Less than 2% with the autotuner
Biological feedback	
Controlling the microwave output by real-time temperature data from up to 16 nonperturbing probes	
Accuracy	0.1°C.
Temperature sample rate	0.5 Hz.
Loop response	2 seconds
Black-and-white and color video temperature display	

energy is transmitted, scattered, reflected, and so forth with respect to species of molecules and characteristics of structure very closely related to the physiological functions of those molecules and structures. It makes biological sense to use it as an interrogating source. This contrasts, for example, to ultrasound tomography, which depends primarily on the tissues' acoustic properties or with x-ray tomography which depends on distributions of the atomic species within molecules and tissues.

DR. JAMES FRAZER: On May 14, 1979, at the University of Maryland, Dr. Prohousky of Purdue University will discuss acoustic transmission through important biomolecules, and we have been missing a bet in acoustic spectroscopy for a long time so far as macromolecules are concerned. However, the rest of Mr. Hunt's comments are, of course, true. One can now noninvasively determine functional specificities using microwaves that one simply cannot obtain any other way. About three weeks ago, HEW Secretary Joseph Califano announced an assault on the use of medical x rays because of possible damage to the patient. Whether or not such damage exists is beside the point. The relative risk is, I think, far less with microwaves than with ionizing radiation. That alone should justify much further development of this particular field. The possibilities are almost limitless.

MR. RICHARD REIS: Dr. Pollack mentioned the longevity of pacemakers. Pacemakers now last five to 10 years because of lithium batteries. Intrinsic device reliability has been a much more significant problem in pacemakers than electromagnetic interference and it is important to put it in that perspective.

So far as the observed effect of interference during our experiments goes, we were using a walkie-talkie to transmit from our receiving station, where we were monitoring the pacemaker that we were studying, back to the transmitting station. We could not monitor while we were using the walkie-talkie because it interfered with our sensitive instruments.

I ask Dr. Pollack to give a little bit of background on the Russian response to our queries on irradiation of the American embassy. I imagine that we asked them why they were irradiating us and so forth, especially in view of their lower standards.

DR. HERBERT POLLACK: In the first place, they have tentatively increased the standard to $5\mu W$, which automatically puts all the maximum chancellery radiation before June of 1975 in the safe level. This is a very important political step as well as a scientific one. Why they were doing it they have never told us. That is one of the secrets that they maintain.

MR. ALAN DROSIN: Mr. Reis, I had the impression that the shielding problem was more serious than you seemed to indicate. Did I misinterpret what you said?

MR. RICHARD REIS: The overall reliability of the pacemaker depends more on other phenomena. There are two critical problems. The first is the unreliability of the battery, specifically the mercury battery, which usually fails in 18 months to two years. The second is the intrusion of moisture into the pacemaker's electronic components. The mercury battery was being improved and it seemed that it would be considerably better, but then the lithium battery came along and it is far better than the mercury battery could be. The other aspect was improved by making the pacemakers hermetically sealed, which had the added benefit of making them slightly less permeable to electromagnetic radiation.

MR. DROSIN: Are you now fairly satisfied with that?

MR. REIS: We still have to exercise some caution in that area. Pacemakers are inherently susceptible to electromagnetic effects, as is any sensitive electronic instrument, particularly in the very low frequency area, where they are intended to be sensitive. The input amplifier of the pacemaker is sensitive from 6 to 80 Hz. Obviously, they will be sensitive to low frequency electromagnetic interference.

DR. NORMAN SIMON (Mt. Sinai School of Medicine): I would like to ask Dr. Frazer a question about his remarkable talk on frontiers in energy. First, the effect of microwave radiation at nonthermal levels does not seem to have been explained as certain at this meeting, whether it is because we do not measure the temperature gradients at nonthermal levels or because it is discrete microscopic temperature and the biological effects appear at higher temperatures, I am not sure. My question pertains to your very interesting exposition of nuclear magnetic resonant image, the cross-section of the chest. Is a thermal effect to be considered even at the energy levels at the same resonance or is it likely that there will not be detectable thermal increases?

DR. JAMES W. FRAZER: There seems little possibility both to get a thermal event and to form a nuclear magnetic resonance image. With electron paramagnetic resonance, however, the frequency is high enough that one could intentionally turn up the power to produce tissue inactivating thermal pulses in a very tightly localized region. That would be a matter of intense localized treatment. One would use nuclear magnetic resonance as a locator, and electron/paramagnetic resonance as a treatment modality. One would, of course, have to be skilled in the use of the apparatus. It is not a job for amateurs.

DR. RUSSELL L. CARPENTER (Bureau of Radiological Health): Dr. Johnson, in applying microwaves locally for local heating, has any incident been made of dielectric lenses which focus the microwave?

DR. RICHARD JOHNSON: Not that I know of. It has certainly been thought of, but I don't know of any studies. Maybe Dr. Gandhi knows.

DR. OM P. GANDHI: No,. not to a large extent. I have seen some reference to this, but not in the context of hyperthermia.

DR. JOHNSON: Dr. Frazer keeps talking about resonance. Is he talking about specific molecular resonance, because I do not think that this exists and if it does exist how do we know when it is going to be specific for humans?

DR. FRAZER: This is nuclear magnetic resonance or electron paramagnetic resonance, which are specific molecular resonances employing both very specific frequencies and an ordering magnetic field. This has nothing to do with the usual discussion of specific resonance frequencies for molecules below approximately 35 gigahertz in the absence of a strong magnetic field. I do not think that such resonances exist in that range, myself, but it is not necessary to invoke resonances in the range below 35 GHz. to produce effects with a high field. George Thurston proved this 10 years ago when he did polarization spectroscopy. Nuclear magnetic resonance has been used since about 1950, since Block and Purcell actually came up with the first successful hydrogen spectrum. It is an identification of chemical species. Alcohol, for instance, has a three, two line spectrum clear to any organic chemistry student. Nuclear magnetic resonance, since its introduction, has become used by organic chemists as a primary means to identify organic compounds. Electron paramagnetic resonance, on the other hand, has been used to follow free radical formations in many processes in tissues and cells and in organic reactions. These are very specific spectroscopic techniques.

DR. ALICE FABIAN (New York State Health Systems Management): Dr. Frazer, has any work been done in activation of viruses, specifically smallpox and polio, in individuals who have received hyperthermia, and what effect does this have on the public health point of view over all?

DR. FRAZER: So far as distinct work in detecting communicable diseases in general, not just the kind of diseases you mentioned, I think it has been totally ignored. In defense of the industry, as it were, I think that the kinds of screens used in experimental protocols would have picked up any widely disseminated disease. They would not have picked up such things as activation of bacteriophage. I think that it is something to examine because an animal is a walking vessel of parasites. One primate becomes a very large number of data points, and gives information on immunologically related coexistence of the host and the parasite. Grinding work, I concede, but it should be taken up. At the moment, there is no such program.

DR. POLLACK: Relative to Dr. Johnson's question, one thing Britton Chance's work showed was that nuclear magnetic resonance analysis can identify molecular species specifically produced by the metabolism of specialized cells. This possibility is being investigated at Yale, using this technique to scan for micrometastases not identified by ordinary diagnostic techniques.

DR. FRAZER: Britton Chance showed ATP, ADP, AMP, creatine phosphate in one scan, which could then be altered by the induction of hypoxia. I am of that generation which would have been jumping around on one leg just for getting the spectrum in a tube, much less in a small part of the cortex of the intact animal. This is a perfectly permissible use of that technique and it should be widely applied. Both Damadian and Bramley and Harris seem to have found specific "tags" for tumor cells that might be exploited.

MR. RON MELNICK (Polytechnic Institute of New York): Is the effect on the phage or on the bacterial cell?

DR. FRAZER: The effect is first on the bacterial cell, then one finds nonreceptive phage incorporation in the first experiment. We melt the bacterial membrane and then introduce the phage. The second effect we demonstrated was on the phage itself, where we had low temperature during radiation and produced noninfectivity.

MR. MELNICK: Are there changes in phage specificity?

DR. FRAZER: We don't know yet. We expect that there are.

MR. MELNICK: Have you eliminated the possibility of latent phage activation?

DR. FRAZER: Not completely. We have in the sense of control survivability of C-600 at the beginning, but I am not absolutely positive.

MR. MELNICK: Do you have to irradiate both the bacteriophage and the *E. coli*?

DR. FRAZER: If one radiates the two together one does not get incorporation. Incorporation and lysis occur only with preradiated *E. coli*.

MR. MELNICK: It seems interesting with the use of microwave tumor therapy. Should any negative aspects be brought out? For example, might internal hemorrhaging develop?

DR. JOHNSON: There are certainly negative effects but not internal hemorrhaging. Temperature measurements of deep structures are difficult. Some vital organs have a very small diffusion rate and can be overheated. Examples are the spinal cord, the eye, and its lens. Any other areas with a very low diffusion rate could be damaged. One requires very well-controlled conditions, and even then hyperthermia is very difficult because of the problem of having really good nonperturbing temperature probes if microwaves are used.

Dr. Frazer, when you discussed the bacteria experiments, were you talking about heat or heat plus the microwaves?

DR. FRAZER: It has been shown that one can cause transitions in the lipid membrane of bacteria with hyperthermia. It depends on the lipid composition of the membrane so that part is simply temperature. The effect on the viral survivability and lower temperature survivability of bacteria was surprising. I thought that we would probably get inactive bacteria on a temperature survivability curve. I am in a quandary myself. We also have conducted these experiments with isolated transfer RNA and we know that single strand RNA is quite sensitive to high amplitude RF fields, I stress that the peak amplitudes were 1 to 3 v./cm. up to 30 v./cm. We controlled the duty cycle so that we did not get marked increases in temperature, but those are very high field gradients. These would be equivalent to something like 30,000 volts per meter in air.

DR. JOHN BERGERON (General Electric): I would like to ask Dr. Frazer or Mr. Hunt to comment on whether or not radiofrequency imaging is possible in the region of dielectric dispersion where there is an appreciable amount of differential in tissue.

DR. FRAZER: I make the following proposition. I think one could do imaging with free access to all of the lovely techniques that Glen Engen has in his department at the National Bureau of Standards, Boulder, Colo., which just happens to include some new double six port analytical schemes for 100 kHz. and up; with free access to that plus the various scanning techniques and computers as used by Paul Wacker and with the addition of short pulse nuclear magnetic resonance, one could envisage very useful developments both in imaging and in therapy.